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Seven decades of vitamin D research in Pakistan : Too little, too much or just right!

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EDITORIAL

Seven Decades of Vitamin D research in Pakistan: Too little, too much or just right!

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Pakistan has one of the highest reported incidence of vitamin D deficiency (VDD) in studies conducted worldwide and within Pakistan. Data mining of vitamin D (VD) testing and small scale community studies from our center in the last decade indicates that VDD in Pakistan is not limited to gender, age group or province [1,2] .Significant correlates of bone health in community dwelling females in Karachi are serum 25-hydroxy vitamin D (25OHD) levels, duration of sun exposure, and wearing veil while determinants of VD levels were identified to be age, town of residence and housing structure. High and low-income localities of both urban and rural environments are identified at risk of VDD. [3,4.] Secondary hyperparathyroidism (sHPT), high bone turnover and other parathyroid hormone related disorders are identified.[5.] GC genotype of R990G SNP of calcium sensitive receptor (CaSR) was found to be associated with higher iPTH levels and lower calcium levels.[6]

Replenishing and maintaining D stores and optimum 25OHD levels to achieve peak bone mass is a challenge. While VD is required for intestinal absorption of calcium, no change in calcium absorption was found before and after VD correction using calcium as surrogate, suggesting the possibility that maximum vitamin D-dependent calcium absorption is achieved in our subjects at a lower 25OHD status, with higher mean parathyroid hormone levels and normal[1], 25 dihydroxy vitamin D levels.[7]

Association of low levels of VD with health or disease has been emphasized a lot over the last decade, while impact of high VD levels has not been studied. Hypervitaminosis D and toxicity is rare and results after prolonged ingestion of large VD doses or use of overzealous VD supplementation with mega dose preparations and can give rise to hypercalcaemia and hypercalciuria.

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Higher mortality rates have been reported at both the lower and upper ends of the 25OHD spectrum. In this context a study in 24,000 adults admitted for acute care by Amrein et al has performed analysis of the association between 25OHD levels measured in the year preceding hospital admission with all-cause mortality after hospitalization. After adjustment for multiple confounders, significantly increased risk for all-cause 90-day mortality was identified in patients with 25OHD level <30 ng/mL or >60 ng/mL, measured before hospitalization, compared to patients with levels between 30 and 60 ng/mL[8]. A U-shaped optimal25OHD range has been proposed for VD. However, it is debated that the reports recommending U-shaped distribution are not representative of findings for disease outcome and are due either to statistical fluctuations associated with low numbers of cases or confounding factors not considered[9].

A review of VD results reported from our laboratory shows increase trend in the results of VD with hypervitaminosis and toxicity (unpublished data). This is also evident in children under 1 year of age.In addition, a recently published study identified 27% of patients admitted to a tertiary care hospital with hypercalcaemia had VD toxicity.[10,11]

Variable practice pattern in treating VD deficiency continue to exist in Pakistan. With the two most commonly available VD preparations in Pakistan, we have shown that single dose of 600,000 IU or 200,000 IU of VD given per oral or intramuscular achieved optimal VD levels in 70% of the subjects after two months of intervention. We have previously demonstrated important implications of dose difference and administration routes in our subjects[12,13]. But due to absence of clear guidelines for the replacement strategies of VD in deficient states, there is inadvertent use of higher doses of VD in patients usually by repeated injectable mega doses of cholecalciferol resulting in hypervitaminosis D and toxicity. In the study by Qamar et al, 27% of the patients with hypercalcaemia were identified to be due to vitamin D toxicity where multiple injections of high dose

preparations were given to these patients and in many it was Vitamin D3 600,000IU injection given weekly for 6-8 weeks.[13]

Life style measures including dietary interventions, education and awareness of pharmacist, physicians, nutritionists, patients and general public is the way forward. The road to bone health and life-long productivity can be achieved through a multidisciplinary approach. There is a need to perform meaningful research to develop local guidelines considering our life style risk factors and available information.

Keywords & abbreviation: Vitamin D (VD) Vitamin D deficiency (VDD), Hypervitaminosis D, Vitamin D toxicity.

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